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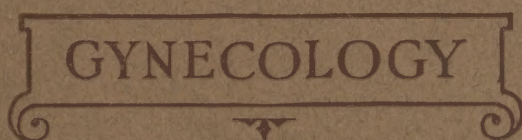


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ORGANOTHERAPY *in* GENERAL PRACTICE

NO.1



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ORGANOTHERAPY IN GENERAL PRACTICE GYNECOLOGY

“THE MOST interesting ‘endocrine crises’

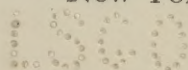
revolve around the sexual factors as does everything in life. One of the fundamental ideas that has been definitely accepted in recent years, in which so many have studied the internal secretions, is the now common one that the various endocrine glands do not act by themselves, individually, but by a close functional correlation, through which, if one gland is affected, others react very quickly, in the endeavor to compensate the disturbance induced in the organism by the former. * * *

If it is certain that the functional unity of the endocrine system makes it impossible for there being a disturbance of any single gland, without the rest participating, it is also beyond a doubt that this repercussion of an originally monoglandular disturbance throughout the entire system, attains its maximum when the gland originally affected is the genital gland. It would appear that the entire endocrine equilibrium depended on the genital function, so that the slightest deviation of the latter is at once betrayed by an immediate disturbance of the system.”—*Maranon*.

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FOREWORD

This monograph on the relation of the internal secretions to gynecology is the first of a series, which it is believed, when completed, will have covered the entire field of organotherapy. It is proposed to devote this series entirely to those applications of organotherapy which are now firmly established and which without doubt will endure in medical practice.

When completed, the series will be assembled and supplemented with sections on general principles, theoretical considerations and an anatomical and physiological description of all the ductless glands, and published as a 256-page book. It is hoped to make this series and the book primarily useful to the general practitioner in his daily practice.

Organotherapy has grown so rapidly and its uses have proved so successful that we feel that the publication of this series is timely and will be well received. Dr. Wm. V. P. Garretson aptly describes the status of the internal secretions in modern medicine:

"The endocrines are functionally basic to all principles of physiology, in fact, endocrinology is physiology, and no physician or surgeon can qualify adequately in any phase of medical science who is failing in knowledge of this subject. We must all be endocrinologists to practice successfully the art of healing which is our paramount function." ("The Interrelation of the Endocrines and the Vegetative Nervous System," Garretson, *New York Medical Journal*, March 15, 1922.)

If this series on organotherapy in some small measure is an aid to the general practitioner our purpose will have been served.

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INTERNAL SECRETIONS IN GYNECOLOGY

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To organotherapy must be given the credit of introducing into gynecology a system of medical treatment as opposed to surgical procedures which had grown and multiplied to such an extent that gynecology in the minds of many physicians came to mean a special branch of surgery. The diverse and apparently unrelated symptomatology encountered in gynecological practice defied explanation and made interpretation in terms of known physiological mechanism impossible. It is not difficult to believe that in the days gone-by the female of the species, with her infinite pains, aches and feelings, received somewhat scant sympathy from our profession, which may too often have regarded as whimsical and emotional these curious syndromes. Endocrinology contributed more perhaps, in its practical application as organotherapy, to gynecology than to any other branch of medicine. The early experimental work of Prenant, Bouin, Ancel, Fränkel, Born, Goltz and others demonstrated without question an endocrine action of the ovary and corpus luteum on menstruation and embryonic development. Further observations on the hypertrophy of the pituitary, thyroid and adrenal cortex during menstruation and pregnancy suggested a function of these glands in the phenomena which later gained general acceptance and contributed to the establishment of the general conception of endocrine interrelationship. With the development of knowledge of the interrelationship of the vegetative nervous system and the endocrine system, there became evident a mechanism sufficient to explain in large part the old, well-known syndromes of gynecology. Endocrine interpretation made organotherapy follow as the logical treatment.

Endocrine Factors and Sex Characteristics

The intimate relationship of the endocrines to the female organism is suggested by the generally accepted views of the influence of the sex glands on the development of the secondary sex characteristics. The embryonic origin of the sex apparatus is undifferentiated. In man about the fifth week the previously undifferentiated genital trace develops into the primary sex organs of one or the other sex. The Wolffian and Muellerian ducts develop up to about the third month of embryonic life without giving rise to the special characteristic morphology of either sex. About this time, differentiation takes place and there arise the special secondary sex organs of one or the other sex. The developing sex cells with their internal secretion influence in marked degree the further development of the organism.* In the male "we are led to the inevitable conclusion that the hormone which gives to the organism its male characteristics is elaborated in the cells of Leydig in the interstitial tissue. In spite of their mesodermal origin, these

*This seems much more probable than that theory which holds that sexual dimorphism is a result of inherent influences from the very beginning — the primordial cell. This theory holds that not only are the sex cells differentiated, but the somatic cells as well. Such a method, however, very probably is operative in the lower orders.

cells are able actively to produce certain specific substances and to transfer these substances to the blood stream; such being the case, we are justified in describing them in their totality as an interstitial gland.

"It is highly probable that by the agency of its secretory products this gland is responsible for the development of the male sexual gland from the primitive genital trace. That it has a determining influence upon the normal development and maturity of the generative portion of the sexual gland, upon the formation of the secondary genital organs and upon the existence and persistence of those morphological and biological characteristics which are the property of the male sex, is undoubted."¹

**Internal
Secretions
Determine
the Sex
Characteristics**

In the female the ovarian hormones determine the development of the secondary sex characteristics and psychic and somatic peculiarities of the female—female type of mammae, skeleton, hair and fat distribution, voice, psyche, etc. "Woman is woman by reason of her generative glands. All the peculiarities of her body and mind, . . . everything in fact which in the true woman we admire and revere as woman, is dependent upon the ovary."²

The work of Steinach has rather firmly established such theory and gives suggestive evidence of the particular part of the sex glands responsible for these profound effects. In his work on male animals, he transplanted testes to other regions of the body. These animals underwent normal development, including the development of the secondary sex characteristics, with sex inclination and libido. On section, these transplanted glands showed atrophy of the spermatogenic elements and hypertrophy of the Leydig (interstitial) cells. If the animal was castrated without transplantation, the secondary sex characteristics and sex desire failed to develop. Steinach's later work in ligating and resecting the vas deferens, with a resulting atrophy or even disappearance of the sexual elements and increase in the interstitial cells, lends further proof that the elements exerting the hormone control are the interstitial cells. A name now familiar, "puberty gland," is applied to the cells taken as a whole. The homologous cells in the ovary are referred to simply as the interstitial cells. Further and even more striking evidence of the influence of these cells upon the development of the secondary sex characteristics is furnished by Steinach's experiments in transplanting ovaries into castrated males of the same species. Here there was a failure of development of the secondary male characteristics and the appearance of certain characteristics of the female—mammary glands, hair, etc.

The foregoing emphasizes the intimate relationship of the endocrines to the sex organs and characteristics of the female and the need for endocrine interpretation in the diagnosis of the disease conditions peculiar to the female genital apparatus. It may be added as an aid to understanding some of the abnormalities of constitution and psyche that irrespective of the course of this differentiation—that is, whether male or female—there remains always some remnant of the opposite sex. Thus in the female the Muellerian duct develops into the oviducts,

¹Biedl, 'The Internal Secretory Organs.'

²Virchow—Biedl's "The Internal Secretory Organs."

uterus and vagina and the Wolffian duct largely disappears. However, part of it persists as the parovarium, the homologue of the epididymis in the male. Moreover, in pseudohermaphroditism both the Muellerian and Wolffian ducts may develop and give well developed secondary sex organs (ducts, external genitalia, etc.) of both sexes in the same individual. Thus, while in general the primary sex cells determine the character and development of the somatic tissues and secondary sex characteristics, certain exceptional forms of development may take place.

Striking Changes of Puberty are Endocrine Effects

At puberty equally striking endocrine effects appear. The phenomena of ovulation, menstruation and pregnancy are inseparably bound up with the internal secretion of the ovary and corpus luteum and are perhaps equally dependent, if not so directly, upon the thyroid, the pituitary and the adrenals. The thymus is of importance also as an endocrine organ and the period of puberty is important in its developmental history. The thymus influences bony growth and is in apparent opposition to the sex glands. In castration and hypoplasia of the genital glands, there is continued development of the thymus. The relation of the ovaries to menstruation was one of the first to be investigated and the results of such research leave no doubt as to the causal relationship. Following the removal of both ovaries there is complete cessation of menstruation, which may be reestablished by grafting an ovary under the skin or in other favorable sites in the body. The further removal of this transplant will again cause cessation of the menses. Such experiments seem effectually to disprove the intervention of a nervous mechanism such as required by Pfleger.

In normal physiology menstruation makes its appearance at the beginning of the period of sexual maturity. In temperate climates, with exceptions for individual and racial variations, this maturity is reached at about the age of fourteen or fifteen years, and menstruation continues as a periodic phenomenon until the time of the menopause—usually from forty-five to fifty years of age. The usual interval elapsing between the menstrual periods is approximately twenty-eight days but variations from this figure are encountered with such constancy that menstruation occurring at intervals of from twenty to thirty-five days may usually be regarded as normal and as not requiring treatment. The period of menstruation is attended by marked changes in the emotional and physical constitution of the woman. Concurrently with the well defined histologic changes occurring in the uterus itself and the “hyperemic wave” which affects not only the uterus, ovary and genitalia but in some degree the whole body, there is definite approach to the maximum of metabolic activity, culminating at the beginning of menstruation and subsiding thereafter. Of the emotional symptoms, the tendency to irritability, lack of self-control, unreasoning attitude and lack of poise is well-known and varies greatly in normal women. In states of abnormal psychology and definite mental and nervous disease the emotional symptoms are intensified. Amenorrhea, the absence of menstruation or menstruation at very irregular periods, is frequently met with in medical practice and demands careful diagnosis and appropriate therapy.

Normally at from forty-five to fifty years of age menstruation ceases and the active sexual life of the individual ends. The ovary is the organ of internal secretion directly connected with menstruation and the premenstrual uterine changes, including the development of the uterus. The effects of the thyroid, pituitary and adrenal cortex are no less certain but are less direct. The results of the removal and transplantation of the ovaries on menstruation have been mentioned. Such removal in the very young animal, before puberty, results in failure of development of the uterus. The exact relations existing between the ovaries and the menstrual phenomenon have been the subject of much speculation. Two theories are worthy of consideration here:

Relation of the Ovaries to Menstruation

1. The explanation offered by Biedl that the interstitial tissue of the ovary furnishes the internal secretion responsible for the characteristic histologic changes of menstruation and of oestrus. In this theory the internal secretion of the interstitial cells is functionally active in the nidation and the development of the ovum after fertilization. A functional antagonism between the interstitial stroma cells and the sex cells is assumed and explains the hypertrophy of the interstitial and atrophy of the remainder during menstruation and pregnancy. This hypertrophy and hypersecretion of the interstitial cells depresses the secretion of the rest of the ovary and accounts for the evidences of ovarian insufficiency at these periods. The theory seems in conflict with generally accepted views at one point, as it assigns to the interstitial cells a function in the local menstrual and reproductive processes only and not in connection with the more profound processes of somatic growth and development.

2. The second hypothesis as to the relations of the ovaries and menstruation is usually referred to as Fränkel's hypothesis. Fränkel assumes that the corpus luteum is the active determining factor in menstruation and the premenstrual uterine changes. Such a relationship had previously been suggested by Born. Fränkel assumes that ovulation takes place about two weeks before menstruation and the resulting corpus luteum furnishes the hormone which sensitizes the uterus and causes the uterine changes characteristic of the premenstrual period. Fränkel's theory, however, is not generally accepted and much evidence at hand tends to disprove it. Ovulation and menstruation frequently occur at times bearing no fixed relation to each other and menstruation may occur independently or without ovulation.

Cyclic changes in the uterus and perhaps other structures of the body undoubtedly take place at the menstrual period, which have been described as premenstrual waves of hyperemia (Dalché). This cyclic phenomenon or tendency may be independent of any effect from the ovary. It is found in lower animals in which the reproductive function is limited to seasonal periods (oestrus) and in which the physical and histological changes both correspond very closely to those in the human female during and before menstruation. In primitive races, there is a resemblance to this lower order condition, for in them there are discernible traces of a tendency to sexual seasons and the period of the menses differs from the usual type. In some, menstruation takes place in one part of the year only.

Frank summarizes the theoretical relation between the ovary and corpus luteum and menstruation as follows:

1. Full maturation of follicles causes the premenstrual changes.
2. Follicular rupture coincides with or follows closely the onset of the menstrual flow.
3. During the active growth of the corpus luteum
 - (a) The uterine mucosa is sensitized, so as to be capable of receiving a fertilized ovum;
 - (b) Follicle ripening is interfered with.
4. During pregnancy the corpus luteum persists; follicular ripening is, therefore, interfered with and hence the menstrual cycle is postponed.

As evidence of the action of the corpus luteum in sensitizing the uterine mucosa and retarding ovulation or the ripening of the follicles, Frank refers to the convincing work of Leo Loeb, who demonstrated in animals that "the uterine mucosa reacts to trauma (foreign bodies, ovum) by producing a decidua which far exceeds in volume the spontaneous oestral or menstrual decidua (experimental deciduomata). If the corpus luteum is destroyed or removed, neither the normal nor artificial decidual reaction takes place; therefore, the ovum cannot be embedded." Loeb found in 66 guinea pigs that spontaneous ovulation rarely occurs within 16 days after a preceding ovulation. In 25 animals all the corpora lutea were successfully removed and in 92% of these ovulation occurred within twelve days after coitus, showing a marked shortening of the interval between ovulations. The presence of a corpus luteum or the injection of corpus luteum extracts into fowls prevents ovulation.

AMENORRHEA

"It is a very great mistake to treat amenorrhea as though it were simply a lack of menstruation, for it is a great deal more than that. Behind this lack lies a cause. It may be in the uterus or the ovaries or it may be still further back in the secretion of the endocrine glands or in the functioning of the vegetative nervous system."¹ The importance of the endocrines in normal menstruation has been described. It should not be assumed, however, that organotherapy is the sole method of treatment or that it is even the method of choice in some cases. Structural defect and emotional influences obviously demand treatment specifically and directly to these causes. Amenorrhea as a result of emotional disturbance is not uncommon and even here the endocrine system may be an intermediary if not a causative agent. Christides² in an article on "Hysterical Amenorrhea" describes such types, and states that in these cases the gynecological condition is improved by recovery from the nervous states. Often there is increased irritability before menstruation, states of anxiety and semi-hysteria. In the greater number of cases of functional amenorrhea an endocrine basis may be demonstrated. In the menstruation phenomenon the ovary is the

¹Dalché, *Revue Française de Gynécologie et d'Obstétrique*, May 1, 1920.

²*Revue Française de Gynécologie et d'Obstétrique*, May, 1920.

endocrine gland immediately concerned but the influence of others, particularly the thyroid and pituitary, should not be overlooked either in diagnosis or therapy. The three *demonstrable* endocrine types are the thyroid, pituitary and ovarian. Engelbach³ illustrates these three types of endocrine menstrual deficiency as follows. They may be studied as type cases of these general classes of amenorrhea.

**Endocrine
types of
Amenorrhea**

Pituitary Type: The pituitary patient had never menstruated. At thirteen she ceased to grow and her facies, bodily contour and lack of secondary sex characteristics remained those of a girl just approaching puberty. Her head was too large for her body and its circumferences not proportioned to one another. From vertex to symphysis she measured two inches shorter than from symphysis to soles of feet. Her height was four inches less than her span. The upper incisors were large and the adjoining canines small. The sella turcica was normal, bones slender, there were no adipose deposits, the thyroid was slightly full.

Ovarian Type: The ovarian patient menstruated regularly and painlessly from thirteen to seventeen. At that age she was suddenly seized with diffuse abdominal pain, tenderness centering at McBurney's point and repeated spells of vomiting, since which she has never menstruated. Removal of the appendix failed to give relief and attacks of migraine with visual disturbances were added to her symptoms; also attacks of sudden edema, dyspnea on exertion and acne of face and chest. She was poorly nourished, tall and slender. Periostitis existed in the right ilium, right femur and both tibia and arthritis in the right sacroiliac joint, accounted for by a 2-plus Wassermann. Luetic treatment for about a year caused the reaction to become negative but during this period her emaciation, abdominal pain, iliac and sacroiliac tenderness, amenorrhea, headaches and vomiting had continued and grown steadily worse. An exploratory operation brought to light no abdominal abnormality and no adhesions. From this on she was given a daily injection of corpus luteum extract and 10 grains of the same preparation by mouth after each meal. Improvement of all symptoms began at once and continued during three years under observation, but menstruation was not restored.

Thyroid Type: The thyroid patient menstruated normally from eleven to fourteen, then began to have irregular attacks of amenorrhea, alternating with normal menstruation. She complained of feeling weak and exhausted, of weak eyesight, of intermittent coccygeal pain and of ecchymotic spots frequently appearing on various parts of her body. She had rickets when a baby and now her upper incisors are large and her upper canines small. She is short of stature and spans some inches more than her height. Her hands and wrists are slender, the epiphyses of radius and ulna not joined to the shafts. Her forehead is low, eyes squinting and deep set, nose of saddle shape with point retroussé, lower teeth crowded a little. No obesity, but breasts, abdomen and mons veneris normally developed; hair in axilla and on mons. Temperament phlegmatic. Thyroid enlarged; sella turcica large.

³*Medical Clinics of North America*, 1920, 665-694.

Engelbach first directs attention to the early personal history of these patients. In pituitary and thyroid disturbances it has little significance but suspicion of prenatal thyroid deficiency should be aroused by a size exceeding ten pounds at birth, by delayed healing of the navel, late eruption of the teeth and deferred walking and talking; also in defective children and those backward at school. Many cases of rickets have been treated with mechanical appliances by competent orthopedists without suspicion of an underlying thyroid cause for the lesion. It is the rule that the hypothyroid girl menstruates at a much earlier age than the normal;* there is a tendency to increase in duration and amount of the flow but without dysmenorrhea. The periods of the eunuchoid girl usually appear after the age of fourteen, are more scanty, of shorter duration and accompanied by more or less dysmenorrhea. The distress, being often located over McBurney's point, is apt to lead to a diagnosis of appendicitis. Nausea, vomiting, backache and extreme malaise are frequent, as they also are with hyperthyroidism.

Individuals of the pituitary type never mature at all or, if they do, late in adult life. In milder cases, the menses may occur at normal intervals but are imperfect in duration and amount and frequently associated with more or less dysmenorrhea and migraine. The history of the eunuchoid type consists in menses that come on after the fourteenth year and are fairly normal at first, gradually decreasing in duration, amount and regularity, accompanied by increasingly severe dysmenorrhea.

In hypopituitary cases there is found an infantile genital tract and absence of secondary sex characteristics. In the eunuchoid the genitals and sex characteristics are properly developed. Thyroid cases usually display a very early overdevelopment in these respects. Insufficiency of ovarian secretion, by withholding the natural antagonist of pituitary and thyroid, permits these latter to cause an overgrowth of the long bones, as seen in the eunuchoid girl. In the other two types this does not occur and consequently there is produced a very short stocky individual. Normally the measurements from symphysis upward and from symphysis downward should be equal. In Engelbach's ovarian case the latter exceeded the former by three inches, the span was the same as the height, although it should have been but double the upper measurement. In the pituitary individual, if disproportion occurs, the upper measurement exceeds the lower.

To a girl whose basal metabolism is thirty per cent. or more below normal, Engelbach gives some preparation containing the equivalent of one-fourth of a grain of extract of whole thyroid three times a day, increasing the dose by one-fourth of a grain each week until the first signs of intoxication appear. Tachycardia above 100 is likely to be the first such indication and the dose which produces it is then slightly decreased and continued for some months until relief is obtained. The ovarian dose must be experimentally ascertained for each individual, beginning at five grains of solid extract and one cubic centimeter of fluid corpus luteum. Stroma and corpus in his experience have proved about equally effective in relieving eunuchoid amenorrhea. Engelbach found hypodermatic administration valuable in both pituitary and ovarian types of cases.

*(This statement has been questioned.)

The amenorrhea of puberty is of a different type from those described by Engelbach. In these cases there is usually involvement of ovaries, pituitary and thyroid and treatment with this combination of gland substances is usually effective. Of this type, Dalché says¹ "The amenorrhea of puberty should not be allowed to go on indefinitely because the sooner it is overcome the easier it is to correct the underlying faults. The fault is lack of stimuli to the ovaries from the thyroid and pituitary but in some cases these fail even with the ovaries added and it is strange but secretion of the prostate and testicles will sometimes prove efficient when these others fail."

**Organotherapy
in Amenorrhea
Usually
Successful**

Treatment: The determination of the glandular type of the amenorrhea is important and is valuable in determining the treatment. While it is true that practically all cases respond better to pluriglandular combinations of ovary, pituitary and thyroid, the diagnosis of predominating fault in any individual gland suggests supplementing the therapy by additional dosage of this particular gland substance. In many instances, as found by Engelbach, hypodermatic administration forms a valuable supplementary treatment. The time element in the treatment of amenorrhea is important, in view of the cyclic elements in menstruation. The maximum therapeutic effort ordinarily should be made just before the estimated time of the menstrual period, in order to take advantage of the combined results of both the therapeutic agent and the cyclic premenstrual changes. In considering ovarian therapy it must be remembered that the interstitial cells of the ovarian stroma and the corpus luteum have very probably different physiological functions. The corpus luteum appears without doubt to have an action in sensitizing the uterus for the reception of the ovum, while the interstitial cells seem to exert a trophic influence. These differences in normal function are reflected in organotherapy by the use of corpus luteum and ovarian residue in the various gynecological syndromes. Thus, Hirst, J. C., in the *New York Medical Journal* of Oct. 5, 1921, advocates *whole ovary* in:

1. Natural menopause;
2. Surgical menopause;
3. Late establishment of menstruation;

Ovarian residue in:

1. Late development of puberty;
2. Infantilism;
3. Irregular menstruation at puberty;
4. Menorrhagia of youth;
5. Obesity and amenorrhea;

Corpus luteum in:

1. The control of the nausea of pregnancy;
2. Habitual abortion without demonstrable cause;
3. Menopause (less efficient than whole ovarian extract);
4. Scanty menses or functional amenorrhea of youth;
5. Pruritus vulvae in elderly women;
6. Sterility.

¹ *Revue Française de Gynécologie et d'Obstétrique*, May 1, 1920.

Summary of Treatment:

1. For routine treatment of functional amenorrhea without predominance of symptoms of a particular gland, Hormotone (thyroid-pituitary-gonad formula) should be given in a dosage of 1 or 2 tablets three times daily. The synergism existing between these gland substances is one of the established facts in organotherapy. Hirst says:

"I believe that the future development will be along the line of pluriglandular therapy, due to the probable correlation between the pituitary, thyroid, mammary gland, suprarenal and ovary, rather than in the use of single extracts."¹

2. When predominance of symptoms points to a well marked gland type, such as described by Englebach, — ovarian, pituitary or thyroid — use Hormotone in a dosage of 1 or 2 tablets three times daily, supplemented by a minimal dosage of the particular gland substance, which may be increased to full therapeutic dosage, to be determined in each case. The desirability of combined gland therapy is recognized by Graves in describing the pituitary type of case:

"In gynecological practice extracts of the whole gland are indicated in menstrual disorders that are essentially the result of pituitary deficiency, in which cases ovarian therapy may be used in combination."

3. In some cases it may be necessary to resort to hypodermatic administration of corpus luteum, solution of posterior pituitary, etc., as supplementary treatment to Hormotone.

CASE REPORTS—Amenorrhea

Rochester, Mich.

"I have just finished using the 100 Hormotone Tablets you sent me as a sample on a very intractable case of amenorrhea of long standing, the patient going 3, 4 or 5 months between periods. She reported today that the last two periods have been normal, 28 days apart and satisfactory in every way. I want to thank you for the opportunity to use Hormotone and wish you would send me 500. I will remit on receipt of bill."

Co. Cork, Ireland.

"I found your Hormotone wonderfully beneficial to a patient who, though not pregnant, had ceased to menstruate, had bronzing of the skin, falling hair and very marked asthenia, showing, to my mind, general failure of function of the ductless glands. After using Hormotone for some time, she has begun to menstruate and her other symptoms show similar improvement."

Birmingham, England.

"A young lady, Miss K. F. —, aged 17½, consulted me. She was a junior school mistress and her chief symptoms were: gradual loss of flesh — she only weighed 5 st. 12 lbs. — amenorrhea for some months, some pigmentation of skin. She was unable to do her school duties and I advised her to obtain 6 months leave of absence. She was seen by a

¹ "The Comparative Value of Whole Ovarian Extract, Corpus Luteum Extract and Ovarian Residue in Menstrual Disorders," J. C. Hirst, *New York Medical Journal*, October 5, 1921.

leading consulting physician and also the chief school medical officer. There were no other symptoms, urine normal. The possibility of Addison's disease was discussed and negatived, and we came to the conclusion she was suffering from some obscure 'internal secretion' insufficiency. To cut a long story short, we put her on your Hormotone tablets and she soon began to improve and after about twelve months' treatment now weighs 8 st. 7 lbs., menstruation regular and has returned to her work."

DYSMENORRHEA

Dysmenorrhea an Endocrine Disease

Dysmenorrhea is painful menstruation occurring at the time of the menstrual period and distinguished from oozing, bleeding and abnormal uterine conditions characterized by pain during the interval between the periods. As a definite disease, dysmenorrhea may be regarded as an endocrine disease, for in those gynecological conditions such as malposition of the uterus, elongated cervix, uterine structural changes, etc., dysmenorrhea is a term descriptive of a symptom, pain, rather than a disease itself. In considering the etiology of dysmenorrhea the various structural or mechanical defects should first be considered. In those cases of determinable defect such as malposition of the uterus, antelexion, faulty development of the uterus, etc., surgery is indicated. It seems certain, also, that although dysmenorrhea is no longer believed in most cases to result from damming back of menstrual blood as a result of stenosed, infantile, cicatricial or flexed cervix, these causes are active in a sufficient number of cases to warrant an examination especially for them before attempting treatment by organotherapy. Operative procedures in cases of these structural abnormalities are usually sufficient to afford relief from the pain. Aside from all these conditions of malposition, infantile uterine development, etc., there remains that large class of cases of dysmenorrhea in which such defects are not present, and in which the cause must be sought for in the functional mechanism of the menstruation process.

The character of the pain in dysmenorrhea is suggestive of the underlying pathologic condition — a spastic, intense contraction of the uterus. This condition seems to prevail uniformly in the several types of dysmenorrhea, regardless of the cause. The pains may be of short duration or persist throughout the menstrual period. They are cramp-like, frequently accompanied by desire to flex the thighs on the abdomen, and accompanied by emotional disturbances which may be severe. These psychic disturbances incident to menstruation may become greatly aggravated. The mental condition is one of unrest and apprehension. Vomiting, headache and anorexia are common.

Before assigning endocrine dysfunction as an etiological factor in these cases some mention should be made of the neurogenic theories of the cause of dysmenorrhea. Various attempts have been made to explain the condition by excessive irritability of the uterus, by nervous stimuli and as a psychoneurosis. There has been a lack of general acceptance of any such views and a marked tendency to an endocrine explanation. It is not improbable that the endocrine factor involving

several of the associated endocrine glands may also involve the nervous system. The intimate relationship between the vegetative system and the endocrines suggests such a possibility, although it is uncertain whether the primary causative factor is in the vegetative nervous system or in the organs of internal secretion. The character of the symptoms of dysmenorrhea strongly suggests that both these causes are associated in the condition. Treatment by organotherapy by its successful results suggests that the endocrine defect is primary.

**Striking
Success of
Pluriglandular
Therapy with
Increased
Dosage of
Ovarian
Substance**

Treatment: Those cases with anatomic defect, malposition, stenosed cervix, etc., require appropriate surgical intervention, the result of which is usually good. In the endocrine cases pluriglandular therapy has been remarkably successful. To the ordinary dosage of thyroid and pituitary, ovarian substance in much larger dosage may be added. The value of ovarian therapy in these cases is especially good and the statement of

Graves is typical of the experience of a large part of the profession:

"The author has recently had striking success in a number of dysmenorrhea cases with a preparation of desiccated ovaries of pregnant animals, minus the corpus luteum. The most marked effect of the extract is seen in its influence on the headache, nausea and vomiting from which many dysmenorrhea patients suffer."

Graves has had marked success in the use of ovarian residue and with extracts of the entire ovary and notes that his results compare favorably with those of physicians who have used the corpus luteum preparations. As to the various ovarian products used, he says:

"Thus it happens that there is a very wide divergence of opinion among clinicians in the matter of ovarian therapy. Many assert that the administration of ovarian substance is entirely valueless in any condition. Such testimony may, however, in the light of recent experience be disregarded. The chief controversy lies in the question as to which part of the ovary is most efficacious therapeutically, some advocating the corpus luteum alone, others the entire ovary, while, as will be seen, the author recommends the ovarian substance from which the corpus luteum has been excluded. Experience shows that all these three preparations have essentially similar physiologic effects when used in certain conditions, variations occurring only in the intensiveness of the results. It may be said that in all preparations the most striking results are obtained in the treatment of the vasomotor symptoms of the menopause. All of them will benefit a certain number of cases of amenorrhea and oligomenorrhea and of circulatory disturbances of the external genitals. It seems probable, therefore, that the active substance is the same, whether the extract be made from the corpus luteum or from the rest of the ovary. Therefore, in selecting a part of the ovary for the extraction of the secretory substance,

it is a matter of choosing that tissue which shall yield the substance in greatest abundance, and with the least toxic effect on the patient.

Present knowledge indicates that there exist both in the corpus luteum and in the atretic follicles cellular elements identical in their origin from a specific connective-tissue structure (the theca interna) and capable of producing an internal secretion which is important to the growth and normal functioning of the organism. If this is true, we have a basis on which to found a rationale for ovarian therapy.

If an internal secretion is manufactured from both the corpus luteum and the atretic follicles by cells of identical structure, extracts made from the corpus luteum alone lack that valuable part of the secretion which is derived from the atretic follicles. Moreover, it is impossible to tell by inspection whether a given corpus luteum is in the process of maturation or at the height of its development, or in a stage of involution and disintegration. It must happen that in the preparation of many corpora lutea for therapeutic purposes a varying number are included in which the essential cells are no longer active as organs of internal secretion, and are actually in a condition of dissolution. We should expect, therefore, that commercial preparations of corpus luteum would present a wide variation in their therapeutic effects, and, owing to their readiness to decompose, would have a special tendency to become toxic.

On the other hand, if the preparation be made from the whole ovary, including corpus luteum, stroma and follicles, the important follicular secretion is not lost. Preparations of this kind would be expected to be more stable in their composition and more constant in their effect than those of the corpus luteum alone. These conclusions have been amply borne out by our clinical experience."

Summary of Treatment: Organotherapeutic treatment by means of thyroid, pituitary and gonadal substance is usually effective. The dosage of the ovarian substance — whole ovary, corpus luteum or ovarian residue — may be relatively larger than that of the others. Hormotone should be given in a dosage of 1 or 2 tablets three times daily and may be supplemented by 1 tablet of Ovarian Comp. t. i. d. or by one 5-grain tablet of corpus luteum, whole ovary or ovarian residue.

CASE REPORTS—Dysmenorrhea

Scranton, Pa.

"Miss —, 26 years old, suffering from dysmenorrhea, was frequently advised by surgeon to undergo operation but refused. Later an operation was necessary for the removal of the vermiform appendix but it was found that the ovary was not involved. The dysmenorrhea continued, however, with great suffering at each period. The patient was put on 4 Hormotone tablets per day and by the end of the second month showed very marked improvement. She is still using the Hormotone (now in the third month). She has menstruated twice since the

Hormotone treatment was begun, the first period showing decreased pain and the second being without pain."

Leeds, Yorks., England.

"I have had some startling results with your product Hormotone. A married woman who regularly menstruated suffered agonies every month. This commenced at the age of 16 and continued up to the time I put her on Hormotone. She is now 27. The pains lasted 24 hours and she was quite unfit for her domestic duties. I put her on Hormotone thrice daily before meals, three days before the expected period. She has had two periods since. With the first there was acute pain for 3 hours and with the second half-an-hour. This after 11 years of most intense suffering. Needless to add, she has become a firm believer in the 'little pink tablets.' Her general health has also improved very considerably."

Waterloo, N. Y.

"It is not my habit to give a testimonial yet I cannot refrain from reporting a case of a young married woman (age 21), one child, who came to me with a history of dysmenorrhea with great prostration at periods and severe chronic headache and hysterical tendencies for past year. After a course of 100 Hormotone tablets she reports feeling fine, last period normal, no headache or hysteria since."

Grand Rapids, Mich.

"Have used this preparation (Hormotone) in a variety of conditions and in one patient in particular I have noted a most remarkable change; a slight discussion might be of interest to you. The patient, M. W. B., age 30, always has complained of trouble in region of ovaries, uterus and tubes as long as can remember. Had operation — abdominal — in 1911. Appendix removed, also left ovary. Was improved after this operation for a short time but continued to be very nervous, with pains throughout abdomen and headache, menstrual periods always extremely painful. In 1915 she had D. & C. operation, with very slight results. Always, following operation and up to present time, never healthy, plenty of ambition but unable to do any amount of work. At times had considerable difficulty with her stomach. Menstrual periods often every two weeks. Had curettement January, 1920, for same condition as previous operations, no great improvement. Pains through abdomen, localized in lower abdominal region. Patient appears very anxious and nervous, at least 10 years older than her age indicates. Has been taking Hormotone tablets for the past three weeks, and we have a most striking difference in her whole bearing. Pains are practically eliminated, menstrual condition is practically normal, only slight pain, not tired or nervous as previous and generally has a bright outlook on life."

MENORRHAGIA

Practically all Menorrhagias Due to Disturbances of the Internal Secretions

process or period.

Prolonged or excessive menstruation is termed menorrhagia. It is descriptive of abnormal alteration of menstruation and refers to a condition occurring at the menstrual period, thus differing from metrorrhagia, which refers to loss of blood from the uterus independent of the menstrual process. The quantity of blood lost varies largely with

individuals and the presence of symptoms such as excessive prostration, anemia, etc., may serve to classify a flow as menorrhagia in one individual that in another would constitute a normal menstruation. Menorrhagia may be due to structural defects, uterine fibroid, pelvic congestion, etc., but its underlying pathology is usually endocrine. The particular site of the endocrine defect is not established with certainty although the ovary appears in all theories to be regarded as a prominent factor. Some authorities have attributed to other glands of internal secretion a very prominent part, but in all theories the immediate effect of ovarian dysfunction is recognized. Meyer-Ruegg¹ expresses a view which, in one form or another, is widely held. Without clearly defining the etiologic factors, this theory holds in general that causation is complex and due to involvement of several of the structures concerned, at the same time clearly recognizing the importance of the ovary as an intermediate factor. In discussing menstruation, its causes and abnormalities, he says:

"It is not at all probable that these changes originate in the ovaries and it is much more probable that they are in consequence of the reciprocal relationship between the other glands of internal secretion, including the mucous membrane of the uterus and nervous system. That the disappearance of menstruation is directly due to changes in the ovaries is improbable because these changes are inconstant on the part of the ovary and because hemorrhages occur either with or without them, and because these same changes exist in the ovaries with or without hemorrhages. Furthermore, we are not sufficiently informed concerning the microscopic anatomy of the ovary during the different phases of its activity to enable us to determine what are physiologic and what are pathologic conditions. The same is true of the mucosa of the uterus. In the ovary we have a very important center which may be regarded as a relay station for influencing the processes in the uterus, and yet to explain uterine hemorrhages and more particularly to explain the arrest of bleeding we must chiefly refer them to local conditions, that is to say, to the mucosa itself."

Graves places greater emphasis upon the ovary as the causative factor and this appears to be the prevailing opinion. Graebke has pointed out that although the hemorrhages of puberty and the climacteric have been attributed to the ovary it is only recently that the hemorrhages which occur in the period of active sexual life have been explained in this way. Former explanations have included metritis, endometritis, hemorrhagic hypertrophy of the glandular mucosa, etc. The influence of the ovary was made evident by the work of Hitschmann and Adler, who demonstrated that the hypertrophy of the uterine mucosa, which had been regarded as pathologic, was a normal premenstrual condition and that both normal and pathologic changes in the uterine mucosa and typical and atypical menstrual hemorrhages were of ovarian origin. The evidence seems clear that the ovary is a most important factor in

¹*Schweizerische Medizinische Wochenschrift*, March 25, 1920.

these conditions, and that the ovarian dysfunction may be either primary or secondary to primary defects in the thyroid or pituitary. Graves says:

"It is not at all unlikely that the menstrual disorders of the climacteric as well as those of the menarche are the result of irregularities in the hormones of the ovaries. It is thought by some that practically all menorrhagias are caused ultimately by a disturbance of the internal secretion of the ovary, and there is much evidence that this is true."

Treatment: Hormotone in a dosage of 1 tablet three times daily may be used for a regulatory influence. The restoration of normal function in the thyroid and pituitary may remove the condition. In cases manifestly of thyroid or hypophyseal origin, these extracts may act promptly in controlling the flow, and as a rule should be given as supplementary dosage to Hormotone. Mammary extract and pituitary substance are both of value by reason of their pharmacological action on the uterus and for this purpose may be used as supplementary treatment. Thymus substance has also been used for this purpose, but its uses are not as well established and its action certainly not comparable with mammary. Osborne says:

"The only use for extracts of the mammary gland is in the profuse menstruation of young girls and young women, and in menorrhagia occurring at the time of the menopause, in other words, in functional bleeding. If there is a local organic reason for the increased flow, of course, it should be treated by proper local methods, but when a young girl floods, or menstruates every two or three weeks, and profusely, mammary tablets, two or three a day, beginning one week before the expected period, will very frequently postpone the period to the normal time. It is also advisable to begin on the third day of a profuse menstruation and give the girl three or four tablets a day, which will often shorten the period. Menorrhagia at the menopause may be stopped in the same manner."¹

Such treatment by mammary and pituitary extracts, however, is symptomatic and should be used as adjuvant treatment to organotherapy by Hormotone or Hormotone and ovarian substance, which attempts to correct the underlying endocrine defect. For such purposes Mammary Comp. in a dosage of 1 or 2 tablets t. i. d. may supplement Hormotone.

METRORRHAGIA

Metrorrhagia is a term descriptive of loss of blood from the uterus in the intermenstrual period. It has no relation to the bleeding of the menstruation process and may be due to tumors, cancer, disease of the endometrium and similar causes. Careful physical examination should always be made in metrorrhagia to determine the local cause. The treatment is surgical and in those cases with etiology similar to menorrhagia the treatment is the same. The symptomatic treatment is by means of mammary and pituitary substance. Mammary Comp. in a dosage of 1 or 2 tablets three times daily should be administered.

¹"Principles of Therapeutics," 1921, Osborne.

CASE REPORTS—Menorrhagia and Metrorrhagia

London, England.

"I am greatly obliged to you for the Hormotone tablets sent me for trial. You will be interested to know that I have tried it since in several cases with very good results. One was a case of persistent dysmenorrhea completely relieved by Hormotone, this case is still under a modified regime of Hormotone tablets. A second case was one of menorrhagia, which has been relieved partially by ovarian extract and completely by Hormotone. Another case that was very thoroughly benefited from the tablets was one suffering from distressing symptoms of the menopause. I may say that in all these cases I was led to believe that the conditions arose from glandular insufficiencies and these conclusions were happily gratified by the results."

Friars Point, Miss.

"I feel that it is my duty to report to you the following case: Mrs. M., 48 years old, entered into the menopause 3 years ago. She had suffered with various circulatory symptoms, such as sleeplessness, vertigo, indistinct vision, cold hands and feet, buzzing sounds and vicarious hemorrhages. Three months ago a persistent metrorrhagia asserted itself and nothing that was done seemed to check the flow. She was seen by several good gynecologists, one of whom diagnosed cancer, the other a uterine neoplasm. She was put on Hormotone, 1 tablet three times a day. To my surprise and gratification, the hemorrhage stopped entirely on the third day, and by the end of the first week's treatment the other objectionable symptoms had disappeared. I was very much gratified at the results I got in this case, and shall continue the use of Hormotone in my gynecological work."

Lake Providence, La.

"Shortly since you were gracious enough to send me 100 Hormotone, and I desire to express sincere appreciation. I had a case just in hand at the time. It was metrorrhagia of long standing. Had all the local physicians (save myself), who assumed it was carcinoma. I used the Hormotone you gave me with the result that the woman is perfectly well today and says she never in her life felt so fine. Priorly she had also received hospital treatment."

MENOPAUSE

The Menopause a Critical Period of Readjustment Involving the Endocrine System

At an age of from forty-five to fifty-five years the active sexual life of a woman comes to an end. Menstruation ceases and the metabolism, habits and psyche undergo changes varying with the individual. The menopause or climacteric is not a sudden transition from one state to another. Only in the most exceptional cases does menstruation end definitely, finally and abruptly. Usually the flow at the periods becomes progressively more scanty, the character of the blood changes and after a somewhat extended period of irregular abnormal menstruation the flow finally ceases.

The menopause includes much more than mere cessation of menstruation or the immediate changes connected with it. A comprehensive study includes consideration of the metabolism, psychic and mental changes and readjustment extending over a long period of the woman's life — a period characterized by Marañón as "the critical age."

"The menopause is not merely a syndrome of genital insufficiency as we believed until recently, but the biological and clinical consequence of a complex and immutable endocrine condition as is that of puberty, the glandular factors of which can be determined with some degree of exactitude, and this fuller knowledge of the mechanism of the condition allows us to explain clearly and to deal accurately with many details of the phenomenon of the climacteric that formerly appeared to us to be full of uncertainty. From this viewpoint, the classical concept of the menopause as a simple genital condition in women has disappeared and in its place there arises a much more comprehensive concept of the critical age — that is, of a long period of the life of both sexes, the principal factor in which is the genital apparatus, but in the development of which all the organic activities play a part."

The menopause may be a period of tranquility, but undoubtedly the greater number of women experience some disturbances which require the attention of the physician. Hot flushes, vasomotor symptoms, dizziness, emotional disturbances and even well marked psychoses may be encountered. The central gland element in the changes of the menopause is undoubtedly the ovary, but it is certain that the associated glands by their reciprocal action largely influence the clinical picture. The relationship of the ovary with these associated glands, which are principally, at least, the thyroid, adrenal and pituitary, has been firmly established, and it is not difficult to assume that at a period in which the action of one essential member of this associated group is removed there will be a consequent and determinable alteration in the functional activities of the remaining members of the group. As a matter of fact, many of the signs and symptoms of the menopause are referable directly to glands other than the ovary. One class of symptoms (vasomotor) of the menopause is so conspicuous that it has been held by many writers

**Vasomotor
Symptoms
Due to
Adrenal
Predominance**

that almost all abnormal changes of the menopause may be explained in terms of such disturbance. Culbertson¹ studied the condition from this viewpoint. He conceives the menopause to be a functional disturbance of the endocrine system dependent upon the withdrawal of the ovarian secretion. Vasomotor disturbances are characterized by an instability of arterial tension and usually this appears as a "vacillating hypertension both systolic and diastolic." The hypertension is assumed to be due to a relative predominance of the hypophysis or the adrenals. The diastolic pressure is not increased to the same extent as the systolic, and the resulting larger pulse pressure is the immediate cause of the symptoms

¹*Surgery, Gynecology and Obstetrics*, December, 1916.

associated with the vacillating arterial pressure. The psychic symptoms appear to be most closely related to change in thyroid function and in the majority of cases hyperthyroidism takes place. The effect of organotherapy in reducing the blood pressure is taken as evidence that the hypertension is functional and not due to structural changes in the body. Such findings as those of Culbertson are found with the greatest frequency in the literature, and it seems beyond question that a large part of the clinical picture of the menopause is due to the predominance of the adrenal effects in raising blood pressure — effects which are in part due to the hypophysis and thyroid, which result from the withdrawal of the inhibiting effect of the ovarian secretion.

The views of the relationship of the ovary to the menopause held by Marañón are worthy of consideration here. He is not in agreement with the theory that the ovary is the primary internal secretory organ at fault at this time but believes that the changes in the ovary are preceded by changes in the other endocrine glands.

"The continuous changes in the activity of the various endocrine glands in the course of life, which prepare the way for a certain event which may occur spontaneously or may supervene in consequence of the occurrence of other and external causes (emotions, various diseases, etc.), are the beginning of the functional decay of the ovary."

As an additional factor in increasing the blood pressure, Marañón includes withdrawal of the hypotensive effect of the ovarian secretion. Such an effect of the ovary he regards as conclusively proved and the combined action of these two factors, gradual withdrawal of the hypotensive action of the ovary and relative increase of the adrenal activity, account for the increased vascular tension and particularly for the unusual variations in pressure, the variability resulting because neither of the two actions is developed uniformly or at a fixed rate. The suprarenal influence he regards as the more important of the two and as of early development in the menopausal condition.

As noted by Culbertson, Marañón, Zondek and others, the characteristic vasomotor disturbance of the menopause is not simple uniform hypertension, but a condition of vasomotor instability. The following summarization of Zondek's views¹ is descriptive of the whole series of vasomotor changes and their relation to the symptomatology: In the climacteric the vascular nervous system is exceedingly unstable. The vasomotor center is in a state of constant irritability. This irritability of the vasomotor center is caused by disturbances in the internal secretions of the ovaries and manifests itself by waves of vasodilatation and pathological distribution of the blood. These waves are characterized by (1) their paroxysmal occurrence, (2) by an initial disturbance in the rhythm of respiration, (3) by a pathological division of the blood. These waves are initiated by an abnormal impulse from the vasomotor center acting upon the vascular district supplied by the splanchnic, causing active constriction of the vessels in this district and driving great quantities of blood into the peripheral vessels. Active dilatation of these peripheral vessels may assist this distribution. The impulses follow

¹*Zeitschrift für Guburtshilfe und Gynäkologie*, June 22, 1920.

each other in rapid succession so that the individual vasomotor effects are not fully developed. As suddenly as they were initiated, so suddenly do they cease, some other impulse taking the place of this one. Then the vasomotor center withdraws the blood from its stasis in the peripheral vessels by active dilatation of the splanchnic vessels, and consequent suction which is supported by vasomotor constriction of the peripheral vessels. Small wonder that these periodic surging waves of vasodilatation and constriction should cause distressing subjective sensations, syncope, palpitation, sweating and states of anxiety and fear. In cerebral efforts the vasomotor center reacts pathologically so that the blood supply so necessary for mental and psychical efforts is not regulated in a physiological manner but abnormally, much as it is in exhaustion or diseases of the nervous system. Physical efforts have a much more normal blood supply. The vasomotor center for heat regulation is frequently abnormal, it does not function in a physiological manner. As a rule, there is a paradoxical reaction to cold.

Internal Secretions and Vegetative Nervous System in Disturbances of Menopause

One other essential factor should receive consideration — the relationship of the vegetative nervous system to those abnormalities other than the vasomotor. In normal individuals the great divisions of the vegetative nervous system — the sympathetic and parasympathetic — are in a state of balanced equilibrium. Their actions are very largely mutually antagonistic and by the nicety of their adjustment afford a mechanism for the regulation of the functional activity of the organs and tissues innervated. The activities of the vegetative nervous system are influenced by the internal secretions and the organs of internal secretion are themselves influenced by the vegetative nervous system. The activities of these two are so intimately connected that disturbance in one must result in disturbance in the other. Now the vegetative nervous system and the endocrine organs are active in the regulation of the functional activity of the vegetative processes of the body, so that the readjustment period is conceivably one in which there will arise not only vasomotor symptoms, but very diverse symptoms referable to the general metabolic activities of the body.

Thus, Mouriquand¹ has described two types of metabolic faults occurring at the menopause, both characterized by obesity, resulting from the disturbed function of the sympathetic nervous system. He describes such symptoms as diabetes, gout, biliary lithiasis, psoriasis, skin disorders, chronic rheumatism, renal and vascular diseases, and loss of tolerance for carbohydrates.

The abnormalities of the menopause are beyond all doubt directly consequent to disturbance of endocrine balance and readjustment in metabolism and function at this period. Much remains to be learned as to the precise changes taking place, but the fundamentals are well established and an endocrine interpretation permits, for the first time, a comprehensive conception of the disturbances of the menopause.

¹*Paris Médical*, May 1, 1920.

Treatment: There are few conditions which have proved as amenable to treatment as the abnormalities of the menopause. This is the more remarkable when we remember that before the development of organotherapy there was perhaps no condition more resistant to treatment. In recognition of the pluriglandular character of the endocrine disturbance as well as by the clinical experience, pluriglandular therapy is indicated. Ovarian substance should be used in the treatment in perhaps larger dosage than in any other condition. Of the value of ovarian substance Graves says:

"The therapeutic value of extracts of ovarian substance has passed beyond the stage of theory and speculation and is now an established fact beyond all doubt. With regard to the nature of the active substance, the exact location in the ovary of its manufacture and many other questions we are still considerably in the dark. The earlier reports of the use of ovarian extracts were, for the most part, discouraging but in recent years better preparations, a more definite knowledge of the physiology of the ovary and a more intelligent selection of cases for treatment have yielded results that are not only satisfactory but often astonishing.

"The value of ovarian therapy is seen in the treatment of patients who are suffering from functional deficiency or absence of the ovarian internal secretion. The most conspicuous examples of this are those who experience the vasomotor disturbances of the natural or artificial menopause, the symptoms of which consist chiefly of hot flushes, vertigo, etc. By the administration of a properly prepared extract these symptoms are, with some exceptions, greatly benefited or made to disappear entirely."

Hormotone should be administered in a dosage of 1 or 2 tablets three times daily, supplemented by 1 capsule of Thyro-Ovarian Comp., which may be increased if the indications demand.

CASE REPORTS—Menopause

Ayrshire, Scotland.

"I am quite satisfied with the results obtained from your Hormotone tablets. I find they do especially well in neurasthenia and allied nervous disorders found in women about the menopause. In such cases the results are very gratifying. I have also used Hormotone in cases of neurasthenia following on nervous shock and business worries with good results."

W. Hoboken, N. J.

"The trial bottle of Hormotone sent me I used on my wife with wonderful results. I have since prescribed it in about a dozen cases of disturbances at menopause with fine results. Each one reports increasing improvement, allowing about two weeks for it to get the right start. In three, it acted almost at once. Undoubtedly, it all depends on the aggravation of the case and, I think, on the degree of anemia that may be present."

Jenners, Pa.

"Some time ago I procured a trial of Hormotone tablets for hot spells in women suffering from the climacteric. They gave prompt satisfaction, so I am placing an order for 500 tablets of same."

Beaver Falls, Pa.

"I am using your Hormotone on a patient, who is going through the change of life, with very good results. She is improving splendidly and the hot flashes are leaving her and she is not nervous like she was before I started it."

Giltner, Nebraska.

"I received a sample of Hormotone a few weeks ago. I gave them to a lady having trouble at the menopause with excessive flowing. They are giving good results. Send me 200 more and send bill of same."

Glasgow, Scotland.

"The supply of Hormotone sent to me a few weeks ago was used by a patient suffering from neurasthenia with neuritis, associated with the menopause. The case was not one in which I expected rapid progress; for some weeks she had been practically at a standstill, with varied reports of neuritis, headache, dyspepsia, insomnia, nightmares, want of appetite, etc. Since using Hormotone, she has certainly made definite progress, though in none of these respects is she free of discomfort. I am of opinion that Hormotone has contributed materially in obtaining the benefit."

STERILITY

Sterility is the term used to describe a condition in the female in which impregnation is impossible. Such a condition is a result of such a variety of causes that any elaborate discussion of the subject necessitates a consideration of a great number of the conditions of gynecological practice as well as the biological conditions underlying absolute sterility. It is a curious fact that in the greater number of the cases in which conception does not take place sterility is attributed to the female rather than the male. There seems little doubt, in view of such investigations as have been made, that the cause should be sought for equally in the male. It is probably preferable that both the husband and wife should undergo examination and that the post-coital examination proposed by Dr. Max Huhner of New York should be carried out.

Four general causes of sterility in the female may be considered: (1) absolute biologic sterility, (2) sterility arising prior to puberty as a result of endocrine defects and resulting hypoplasia of the genital organs, (3) sterility arising as a result of abnormal function of the ovary, the other genitalia being normal, and (4) sterility due to structural defects, infections, etc. Absolute biologic sterility is probably rare.

Supplementing these general classifications of sterility, it is well to consider that in cases in which conditions for fertilization are not ideal various apparently slight factors may determine impregnation. Reynolds and Macomber¹ describe such factors under the title of "Relative Fertility." They point out that such factors as diet, climate, racial characteristics and others influence the problem.

¹ *Boston Medical and Surgical Journal*, March 23, 1922.

The treatment of cases due to structural defect, infection, etc., is surgical or local. In cases with an endocrine disturbance as the cause, organotherapy is valuable. Bandler has had very favorable results:¹

"I am now using extract of the whole ovary, thyroid and ovarian residue with an occasional dose of morphine for threatened miscarriage and the same preparation without morphine for repeated miscarriage, no longer paying exclusive attention to the Wassermann side of the question. The results are so excellent in both these conditions that I consider them the best test and the best proofs of endocrine therapy in the whole realm of gynecology.

"It is only a slight step from this experience to the conclusion that if these gland extracts aid in preserving the contact of the ovum and its continued growth, that they must of necessity have the same power in promoting embedding of many a fecundated ovum which, without this aid, is cast off at menstruation. If these considerations concerning ovary, tube and decidua be true, the way to treat these conditions is clearly pointed out to us. We must substitute those internal secretions which are lacking or we must excite the action of certain of those internal secretions in order to cause the rupture of a Graafian follicle containing a ripe ovum; to give power to the Graafian follicle to secrete an enzyme which will enable it to rupture; to stimulate the lining of the tubes so that the cilia will function and to exert a trophic action on the endometrium which will permit the embedding and retention of a fecundated ovum. In other words, we stimulate by extracts of the glands which normally preside over those functions. On the other hand if the action of the ovaries and associated supporting glands be increased and the patient menstruates too often or too profusely, . . . then we are dealing with endocrines unusually assertive or a uterus too greatly stimulated. Here we must inhibit these stimuli and diminish menstrual function by endocrines or by resection of part of each ovary.

"Although the usual treatment of sterility as I now practice it consists mainly of two preparations of ovarian extract and one of thyroid, let me make mention of a few general considerations. We prescribe according to the patient's local signs, menstrual symptoms and constitutional makeup. We judge from a patient's appearance, her weight, the distribution of hair, character of the skin, cold, clammy hands, premenstrual phenomena, rate of the pulse, blood pressure, as well as of our local findings. Now the glands which stimulate genital function are ovarian secretion itself, thyroid secretion, suprarenal extract, pituitary gland posterior, in some cases probably anterior. The glands which serve to diminish the menstrual function are thymus and mammary, placental extract and in some phases probably thyroid.

¹ *New York Medical Journal*, February 22, 1919.

"When a patient shows signs of myxedema or myxedema of the endometrium is suspected, thyroid is indicated. If patients show signs of hyperthyroidism or exophthalmic goitre, thyroid is not indicated. Patients having a typical dystrophia adiposo genitalis are the victims of a pluriglandular condition. To such patients we give pituitary extract in addition to ovary and thyroid. Patients with low blood pressure and asthenia suggest the administration of suprarenal extract and pituitary extract. Patients with large uteri and excessive menstruation, patients with large ovaries and excessive menstruation, whether these ovaries appear cystic or not, the so called oyster ovary, suggests the administration of thymus or mammary extract or placental extracts or all three."

Bandler reports that out of a series of fifty consecutive cases, twelve patients in which the condition was not due to structural causes have responded to endocrine therapy and eleven became pregnant within three months after administering the gland extracts and one after administration for four months.

Solomon¹ reports that administration of glandular extracts, especially ovary, is useful in appropriate cases.

Treatment: In such cases Hormotone should be given in a dosage of 1 tablet three times daily and may be supplemented with one 5-grain tablet of ovarian substance three times daily or with one tablet of Ovarian Comp. three times daily.

CASE REPORTS—Sterility

Washington, D. C.

"I will again state that my experience with Hormotone has been more than gratifying and I have had surprising results from its use. The two classes of cases I have been most successful with by the use of Hormotone are as follows: The case of sterility resulting from uremic poisoning and premature delivery, which had lasted for about ten years was cured and after taking Hormotone for about two months became pregnant. The most marked improvement and cure of cases of amenorrhea, metrorrhagia and menorrhagia by its use has been my experience."

New Orleans, La.

"Mrs. —, 38 years old, very fat, rather myxedemic, neurasthenic, suffering from hot flashes and pain in the top of her head, had not menstruated since the birth of her first child, a healthy, well developed boy, now twelve years old. The patient and her husband were desirous of more children and did everything possible to aid conception by posture, rest and quiet, consulted many medical men and surgeons, and in general were told that it was a case of early menopause. In October, the patient was ordered to take six Hormotone tablets daily, — two t. i. d. Very soon the attacks of heart palpitation subsided, belching of gas from the stomach stopped and the patient acquired a poise and self-confidence which she had lost; in fact, she had been subject to 'fears' for some time. Her muscles became firmer, cheeks became rosy,

¹*Surgery, Gynecology and Obstetrics*, 1920, XXX, 173.

she lost sixteen pounds weight and seemed to care more for her husband than she had lately. This treatment was continued intermittently until now. Although the patient did not menstruate, she developed a morning vomiting in November and December of the following year and was told she probably was pregnant. Three months later this was confirmed by unmistakable fetal heart sounds. She went through a physiological gestation, no albumen appeared in the urine until a week before delivery, when only a little appeared, her feet did not swell at all—in fact, she went through this pregnancy better than do most younger women. Ten days ago labor pains came on but were weak. The patient's first parturition was accompanied by extensive lacerations and subsequent fibrous scars. These facts—the weak pains and the fibrosis of the perineum—inclined to the decision of cesarean section which was performed successfully and bloodlessly after the method of Dr. Davis, and the patient was delivered of a boy infant which she is now nursing. It is intended that the patient continue taking Hormotone until it is time to wean the child."

SPECIAL FORMULAE

Each formula is sold in bottles of 40 and 100 capsules or tablets

No. 1 Pluriglandular Comp. Male

Hypoadrenia, Asthenia, Low Blood Pressure, Fatigue Syndrome

Thyroid
Pituitary
Suprarenal
Orchic
Physiological Salts Comp.

grs. 1/10
" 1/40
" 1/4
" 1/4
" 1/4

Dose: 1 or 2 capsules 3 times daily.

No. 2 Pluriglandular Comp. Female

Hypoadrenia, Asthenia, Low Blood Pressure, Fatigue Syndrome

Thyroid
Pituitary
Suprarenal
Ovarian
Physiological Salts Comp.

grs. 1/10
" 1/40
" 1/4
" 1/4
" 1/4

Dose: 1 or 2 capsules 3 times daily.

No. 3 Pineal Comp. Male

Backward Children, Mongolism, Retarded Mental or Physical Development

Anterior Pituitary
Thyroid
Suprarenal
Orchic
Pineal
Physiological Salts Comp.

grs. 1/5
" 1/5
" 1
" 1 1/2
" 1/30
" 1/4

Dose: 1 or 2 capsules 3 times daily.

No. 4 Pineal Comp. Female

Backward Children, Mongolism, Retarded Mental or Physical Development

Anterior Pituitary
Thyroid
Suprarenal
Ovarian
Pineal
Physiological Salts Comp.

grs. 1/5
" 1/5
" 1
" 1 1/2
" 1/30
" 1/4

Dose: 1 or 2 capsules 3 times daily.

No. 5 Orchic-Prostate Comp.

Enlarged Prostate, Sexual Neurasthenia, Vesical Irritation

Orchic
Prostate
Calcium Glycerophosphate

grs. 1
" 2
" 2

Dose: 2 or 3 capsules 3 times daily.

No. 6 Corpus Luteum Comp.

Vomiting of Pregnancy (Hyperemesis Gravidarum), Menstruation Psychosis, Mild Manic Depressive Insanity (Females)

Corpus Luteum
Thyroid
Physiological Salts Comp.

grs. 1
" 1/10
" 1/4

Dose: 1 to 3 tablets every 3 or 4 hours, which may be increased to 5 tablets in unusually severe cases.

No. 7 Parathyroid Comp.

Tetany, Uremia, Epilepsy, Paralysis Agitans, Nervous Tremor of Children

Parathyroid
Orchic
Calcium Lactate

grs. 1/20
" 1
" 2

Dose: 2 or 3 capsules 3 times daily.

No. 7 N. P. Parathyroid Comp.

Tetany, Uremia, Epilepsy, Paralysis Agitans, Nervous Tremor of Children

Parathyroid Nucleo Protein
Orchic
Calcium Lactate

grs. 1/20
" 1
" 2

Dose: 2 or 3 capsules 3 times daily.

No. 8 Thymus Comp.

Chronic Arthritis, Rheumatoid Arthritis, Arthritis Deformans

Thymus
Thyroid
Pituitary

grs. 1
" 1/10
" 1/20

Dose: 1 or 2 tablets 3 times daily.

No. 9 Mammary Comp.

Menorrhagia, Metrorrhagia, Subinvolution, Prolonged Menses, Uterine Oozing

Mammary
Posterior Pituitary
Calcium Lactate

grs. 2
" 1/2
" 2

Dose: 1 tablet 3 times daily.

No. 10 Suprarenal-Pituitary Comp.

Asthma, Bronchial Asthma

Suprarenal
Pituitary Entire
Thyroid
Anterior Pituitary
Physiological Salts Comp.

grs. 2
" 1
" 1/10
" 1 1/2
" 1/4

Dose: 1 or 2 tablets 3 times daily, which may be increased when asthmatic aura appears.

No. 11 Ovarian Comp.

Amenorrhea, Ovarian Hypofunction, Menopause.

Ovarian Substance
Thyroid
Physiological Salts Comp.

grs. 3
" 1/10
" 1/4

Dose: 1 or 2 tablets 3 times daily, which may be increased to 3 or 4 tablets from 5 to 10 days before the expected menstrual period.

No. 12 Renal-Pancreas Comp.

Nephritis, Prevention of Uremia.

Kidney Substance
Pancreas
Physiological Salts Comp.

grs. 2
" 2
" 1/4

Dose: 1 or 2 tablets 3 times daily.

IN ONE BOTTLE

IN ONE BOTTLE

TRYPSOGEN	Diabetes mellitus; glycosuria and defective carbohydrate metabolism. Also useful in certain pancreatic disorders, and as an adjunct in hypertension. <i>May be had without gold and arsenic at same prices.</i>	100	SECRETOGEN	A physiological treatment of gastrointestinal insufficiencies and constipation, intestinal stasis, infantile diarrheas, marasmus and inanition.	100
Tablets		500	Tablets only		500
		1000			1000
Capsules		100			
Caps. Dble. Str'ngth		100	Elixir	Tablets. A homeostimulative extract from the duodenum.	1/2 pt.
				Dose: 1 to 3 tablets before or after meals.	1 pt.
				Elixir. A homeostimulative extract from the stomach and duodenum; contains 1/10 of 1% HCL.	5 pts.
				Dose: 1 to 3 teaspoonsfuls before or after meals.	1 gal.

SINGLE GLAND PRODUCTS

Our organotherapeutic products are made from fresh glands of healthy food animals, in our own laboratory, under the supervision of competent chemists. All moisture has been removed from these gland products and they will keep indefinitely until opened. They are hygroscopic and should not be exposed to the air. Keep bottle tightly corked.

	In one bottle		In one bottle
Albuzyme	caps. 75	Ovary w/o	Powder oz.
Amylzyme	Powder oz.	Corpus Lut.	5-gr. caps. 100
	caps. 40		
	100	Ox Gall	Powder oz.
Brain	Powder oz.	Pancreas	Powder oz.
Brain &	2-gr. tabs. 100		5-gr. caps. 100
Spinal Cord			
Corpus Luteum	Powder 1/8 oz.	Pancreatin	Powder oz.
	oz.	(U.S.P.)	2-gr. tabs. 100
	2-gr. tabs. 50		5-gr. caps. 100
	100		
	5-gr. tabs. 50	Pancreatin &	Tablets 100
	100	Soda	
	5-gr. caps. 50		
	100	Parathyroid	Powder 1/8 oz.
1 c.c. ampoules, 20% 1/2 doz.			1/20-gr. tabs. 100
Duodenal Sub.	Powder oz.	Parotid	Powder oz.
Epinephrine	Powder 1 grain		
	Chloride Sol., 1-1000 oz.	Pepsin (U.S.P.)	Powder oz.
1 c.c. ampoules, 1:10,000 1/2 doz.			
Glycogen	Powder 1 gram	Pineal Gland	Powder 1/8 oz.
	1/4 oz.		1/10-gr. tabs. 100
	1/2 oz.		
	1 oz.	Pituitary	Powder 1/8 oz.
2 c.c. ampoules (box of 6)			1 oz.
Kidney	Powder oz.		1/2-gr. tabs. 50
	2-gr. tabs. 100		100
	5-gr. caps. 100		1-gr. tabs. 50
Lecithin	1/2 oz. jars		100
" Commercial	1 oz. jars		2-gr. tabs. 50
Liver	Powder oz.		100
	3-gr. tabs. 100	Pituitary, Ant.	Powder 1/8 oz.
	5-gr. caps. 100		1 oz.
Lymphatic Gl.	Powder oz.		1-gr. tabs. 50
	3-gr. tabs. 100		100
Mammary	Powder oz.		2-gr. tabs. 50
Sub.	3-gr. tabs. 100		100
	5-gr. caps. 100		
Marrow—Red	1/2 pt.	Pituitary, Post.	Powder 1/8 oz.
Bone Glycerole	1 pt.		1/10-gr. tabs. 100
Orchic Sub.	Powder oz.		1/2-gr. tabs. 100
	2-gr. tabs. 100		(Liquor Hypophysis)
	5-gr. caps. 100		1/2 c.c. ampoules, Ob., 1/2 doz.
			1 " " 1/2 doz.
Ovarian Sub.	Powder oz.		1 c.c. ampoules, Surg., 1/2 doz.
	2-gr. tabs. 100		
	5-gr. tabs. 50	Placenta	Powder oz.
	100		3-gr. tabs. 100
	5-gr. caps. 50		5-gr. caps. 50
	100		100

Prostate	In one bottle		Thyroid (U.S.P.) (cont.)	In one bottle	
	Powder	oz.		½-gr. tabs.	100
	2-gr. tabs.	100		1-gr. tabs.	100
Spleen	In one bottle		Tonsil	In one bottle	
	Powder	oz.		2-gr. tabs.	100
	3-gr. tabs.	100		1-gr. caps.	100
Steapzyme	In one bottle		Suprarenal Gland (U.S.P.)	In one bottle	
	3-gr. tabs.	100		2-gr. caps.	100
	5-gr. caps.	100		3-gr. caps.	100
Suprarenal Cortex	In one bottle		Suprarenal Medulla	In one bottle	
	Powder	oz.		Powder	oz.
	1-gr. tabs.	100		1-gr. tabs.	100
Thymus	In one bottle		Thyroid (U.S.P.)	In one bottle	
	2-gr. tabs.	100		Powder	oz.
	3-gr. caps.	100		1/10-gr. tabs.	100
Thyroid (U.S.P.)	In one bottle		Thyroid (U.S.P.)	In one bottle	
	1/10-gr. tabs.	100		1-gr. tabs.	100
	¼-gr. tabs.	100		3-gr. caps.	100

Nucleo-Protein Products

Ovarian	Nucleo-protein	10%
		100 Tablets
Parathyroid	Nucleo-protein	5%
		20 Tablets
Pituitary	Nucleo-protein	10%
		20 Tablets
Suprarenal	Nucleo-protein	10%
		100 Tablets
Thyroid	Nucleo-protein	1%
		100 Tablets
"	Nucleo-protein	5%
		100 Tablets
"	Nucleo-protein	10%
		100 Tablets
"	Residue	½ oz

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Hong Kong, Honolulu, Barcelona and in the important cities of
Central and South America.

BRITISH ISLES—Requests for literature and general information will receive prompt
attention if addressed to
S. C. RITCHIE, 1 Charing Cross, London, S. W. 1.

"By careful observation and analysis of symptoms, both subjective and objective, it becomes a relatively simple matter to interpret endocrine dysfunction. In supplying the deficient gland substances by intelligent therapeutic methods one may promptly create an endocrine balance and eradicate annoying symptoms in a manner that is frequently uncanny and most spectacular, as well as quite impossible by any other therapeutic means at our disposal."—"The Interrelation of the Endocrines and the Vegetative Nervous System", Garretson, *New York Medical Journal*, March 15, 1922.)

The intimate relationship existing between the endocrines and vegetative nervous system makes possible an explanation of the symptoms of disorders of

MENSTRUATION and the MENOPAUSE

which have always been difficult of interpretation. In active sexual life, faulty ovarian, thyroid, pituitary and adrenal function give rise to amenorrhea, dysmenorrhea, menorrhagia, etc. At the menopause, the period of endocrine readjustment, the balance of the vegetative nervous system is affected and the symptomatology frequently urgent. Careful endocrine diagnosis and proper organotherapeutic treatment make the prognosis favorable.

HORMOTONE

supplies the deficient gland substances and meets all the requirements of the best organotherapeutic treatment of these conditions.

When there is associated high blood pressure, use

HORMOTONE WITHOUT POST-PITUITARY

G. W. CARNRICK CO.

417-421 Canal Street

New York, N. Y.

DIABETES MELLITUS

is amenable to treatment and every case should receive more
than attention to the dietary.

TRYPSOGEN

is valuable in the treatment in

Improving the combustion of sugar;
Re-establishing normal carbohydrate metabolism by homo-
stimulation;
Restoring normal intestinal digestion and aiding nutrition;
Depressing a relative adrenal hyperfunction;
Lessening polyuria.

DOSE: One or two tablets after meals. The dose should
be gradually increased to 6 or 7 tablets three times daily.

G. W. CARNRICK CO.

417-421 Canal Street

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The intestinal digestive processes are dependent upon an adequate supply of
the digestive enzymes, the production of which is under hormone control.

Physiological Stimulation

of the natural enzymes of the body by the extracts of the duodenal and
pyloric mucosa is the most effective treatment for restoring normal phy-
siological digestion.

SECRETOGEN

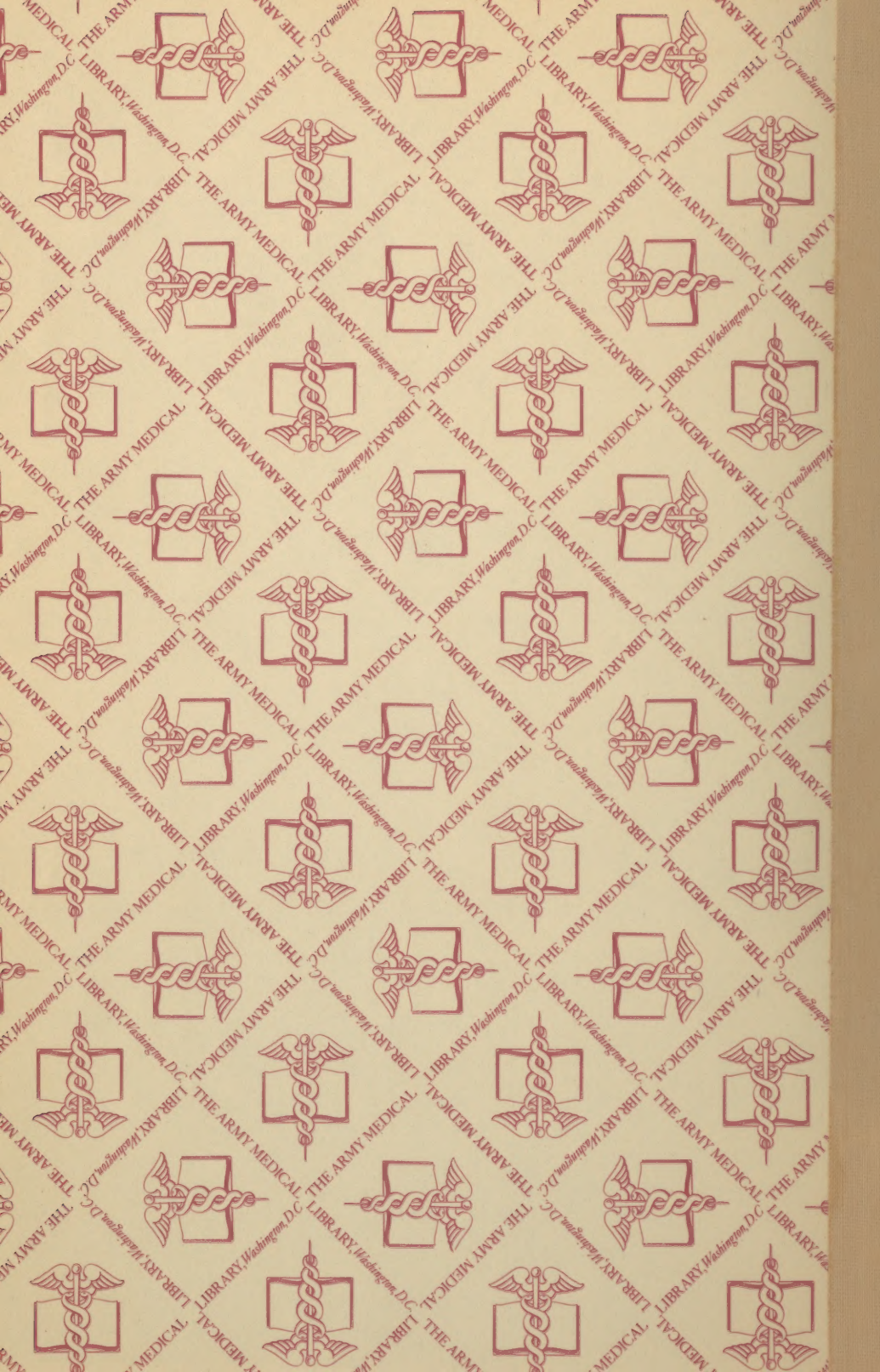
is prepared from the hormone-bearing mucosa of the duodenum, com-
bined with the pro-ferments of the pancreas and pylorus, together with
the enzymes of the peptic glands. It stimulates the production of the hor-
mones exciting the outpouring of the digestive juices and enzymes.

Indications: Atony of stomach, dilatation, fermentative dyspepsia of
the atonic type with flatulence, chronic gastric catarrh of the asthenic
type.

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